=> d his

(FILE 'HOME' ENTERED AT 08:49:22 ON 28 MAY 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:49:32 ON 28 MAY 2002
L1 6875 S (BRCA1 OR BRCA(W)1)
L2 69 S L1 AND (EXON# (5A) (13 OR 22))
L3 34 DUP REM L2 (35 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 08:53:54 ON 28 MAY 2002

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:57:15 ON 28 MAY 2002
L4 53 S T4 AND THERMOLABILE
L5 3 S T4 AND THERMOLABILE (9A) EXONUCLEASE#
L6 1 S T4 (4A) POLYMERASE (8A) (THERMOLABILE OR THERMOSTABLE)

FILE 'SCISEARCH' ENTERED AT 08:59:49 ON 28 MAY 2002
L7 3747 S DWIVEDI?/RAU
L8 87 S L7 AND 221/RVL
L9 1 S L8 AND T4
L10 25 S INACTIVAT? (7A) EXONUCLEASE#
L11 25 DUP REM L10 (0 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 09:05:12 ON 28 MAY 2002
L12 147 S INACTIVAT? (7A) EXONUCLEASE#
L13 7 S L12 AND (CLON?)
L14 5 DUP REM L13 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 09:06:20 ON 28 MAY 2002

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=> d l3 29-34 bib ab
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L3 ANSWER 29 OF 34 MEDLINE DUPLICATE 16
AN 1998016423 MEDLINE
DN 98016423 PubMed ID: 9354803
TI **BRCA1** genomic deletions are major founder mutations in Dutch breast cancer patients.
CM Erratum in: Nat Genet 1997 Dec;17(4):503
AU Petrij-Bosch A; Peelen T; van Vliet M; van Eijk R; Olmer R; Drusedau M; Hogervorst F B; Hageman S; Arts P J; Ligtenberg M J; Meijers-Heijboer H; Klijn J G; Vasen H F; Cornelisse C J; van't Veer L J; Bakker E; van Ommen G J; Devilee P
CS Department of Human Genetics, Leiden University Medical Centre, The Netherlands.
SO NATURE GENETICS, (1997 Nov) 17 (3) 341-5.
Journal code: BRO; 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19990129
Entered Medline: 19971204
AB To date, more than 300 distinct small deletions, insertions and point mutations, mostly leading to premature termination of translation, have been reported in the breast/ovarian-cancer susceptibility gene

BRCA1. The elevated frequencies of some mutations in certain ethnic subpopulations are caused by founder effects, rather than by mutation hotspots. Here we report that the currently available mutation spectrum of **BRCA1** has been biased by PCR-based mutation-screening methods, such as SSCP, the protein truncation test (PTT) and direct sequencing, using genomic DNA as template. Three large genomic deletions that are not detected by these approaches comprise 36% of all **BRCA1** mutations found in Dutch breast-cancer families to date. A 510-bp Alu-mediated deletion comprising **exon 22** was found in 8 of 170 breast-cancer families recruited for research purposes and in 6 of 49 probands referred to the Amsterdam Family Cancer Clinic for genetic counselling. In addition, a 3,835-bp Alu-mediated deletion encompassing **exon 13** was detected in 4 of 170 research families, while an deletion of approximately 14 kb was detected in a single family [corrected]. Haplotype analyses indicated that each recurrent deletion had a single common ancestor.

L3 ANSWER 30 OF 34 MEDLINE DUPLICATE 17
AN 97029994 MEDLINE
DN 97029994 PubMed ID: 8875917
TI Clinical and pathological features of ovarian cancer in women with germ-line mutations of **BRCA1**.
CM Comment in: N Engl J Med. 1996 Nov 7;336(19):1455-6
Comment in: N Engl J Med. 1997 Apr 24;336(17):1254-5; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1254; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1255-6; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1255; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1256; discussion 1256-7
AU Rubin S C; Benjamin I; Behbakht K; Takahashi H; Morgan M A; LiVolsi V A; Berchuck A; Muto M G; Garber J E; Weber B L; Lynch H T; Boyd J
CS Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia, PA 19104, USA.
SO NEW ENGLAND JOURNAL OF MEDICINE, (1996 Nov 7) 335 (19) 1413-6.
Journal code: NOW; 0255562. ISSN: 0028-4793.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961114
AB BACKGROUND: We tested the hypothesis that ovarian cancers associated with germ-line mutations of **BRCA1** have distinct clinical and pathological features as compared with sporadic ovarian cancers. METHODS: We reviewed clinical and pathological data on patients with primary epithelial ovarian cancer found to have germ-line mutations of **BRCA1**. Survival among patients with advanced-stage cancer and such mutations was compared with that in control patients matched stage, grade, and histologic subtype of the tumors. A combination of single-strand conformation and sequencing analyses was used to examine the **22** coding **exons** and intronic splice-donor and splice-acceptor regions of **BRCA1** for mutations in pathological specimens. Alternatively, some patients were known to be obligate carriers of the mutant **BRCA1** gene because of their parental relationships with documented mutant-gene carriers. RESULTS: We identified 53 patients with germ-line mutations of **BRCA1**. The average age at diagnosis was 48 years (range, 28 to 78). Histologic examination in 43 of the 53 patients showed serous adenocarcinoma. Thirty-seven tumors were of grade 3, 11 were of grade 2, 2 were of grade 1, and 3 were of low malignant potential. In 38 patients, the tumors were of stage III; 9 patients (including those with tumors of low malignant potential) had stage I

disease, 5 had stage IV, and 1 had stage II. As of June 1996, with a median follow-up among survivors of 71 months from diagnosis, 20 patients had died of ovarian cancer, 27 had no evidence of the disease, 4 were alive with the disease, and 2 had died of other diseases. Actuarial median survival for the 43 patients with and advanced-stage disease was 77 months, as compared with 29 months for the matched controls ($P<0.001$). CONCLUSIONS: As compared with sporadic ovarian cancers, cancers associated with **BRCA1** mutation appear to have a significantly more favorable clinical course.

L3 ANSWER 31 OF 34 MEDLINE DUPLICATE 18
AN 96225458 MEDLINE
DN 96225458 PubMed ID: 8640237
TI Mutation analysis in the BRCA2 gene in primary breast cancers.
AU Miki Y; Katagiri T; Kasumi F; Yoshimoto T; Nakamura Y
CS Department of Human Genome Analysis, Cancer Chemotherapy Center, Tokyo, Japan.
SO NATURE GENETICS, (1996 Jun) 13 (2) 245-7.
Journal code: BRO; 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D83989
EM 199607
ED Entered STN: 19960726
Last Updated on STN: 19990129
Entered Medline: 19960716
AB Breast cancer, one of the most common and deleterious of all diseases affecting women, occurs in hereditary and sporadic forms. Hereditary breast cancers are genetically heterogeneous; susceptibility is variously attributable to germline mutations in the **BRCA1** (ref. 1), BRCA2 (ref. 2), TP53 (ref. 3) or ataxia telangiectasia (ATM) genes, each of which is considered to be a tumour suppressor. Recently a number of germline mutations in the BRCA2 gene have been identified in families prone to breast cancer. We screened 100 primary breast cancers from Japanese patients for BRCA2 mutations, using PCR-SSCP. We found two germline mutations and one somatic mutation in our patient group. One of the germline mutations was an insertion of an Alu element into **exon 22**, which resulted in alternative splicing that skipped **exon 22**. The presence of a 64-bp polyadenylate tract and evidence for an 8-bp target-site duplication of the inserted DNA implied that the retrotransposal insertion of a transcriptionally active Alu element caused this event. Our results indicate that somatic BRCA2 mutations, like somatic mutations in the **BRCA1** gene, are very rare in primary breast cancers.

L3 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2002 ACS
AN 1997:146761 CAPLUS
DN 126:181894
TI A protein truncation test for **BRCA1**
AU Garvin, Alex M.; Mueller, Hj.; Scott, Rodney J.
CS Dep. Genetics, Children's Hosp., Basel, Switz.
SO Hered. Cancer, Int. Res. Conf. Fam. Cancer, 2nd (1996), Meeting Date 1995, 6-10. Editor(s): Mueller, Hansjakob; Scott, Rodney J.; Weber, Walter. Publisher: Karger, Basel, Switz.
CODEN: 64BIAV
DT Conference
LA English
AB The recently isolated **BRCA1** gene [1] spans 100 kb of chromosome 17q21 and contains 1,863 codons dispersed on **22 exons**. Screening for mutations in **BRCA1** by single-strand conformation

polymorphism (SSCP) or sequencing requires as many as 50 PCR reactions followed by anal. of the 50 amplified products [2]. Such a work-intensive endeavor makes large-scale screening of **BRCA1** problematic. One way of reducing the amt. of work required to screen coding sequence is to perform a protein truncation test (PTT) [3], in which the coding sequence is PCR amplified with an RNA polymerase binding site attached to its 5' end. The PCR product is then used as template in a coupled in vitro transcription/translation reaction and the radiolabeled protein product is analyzed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). PTT has been successful in screening for mutations in the APC tumor suppressor gene [4]. Since 86% of all mutations found in **BRCA1** result in a truncated protein product [5], **BRCA1** is an esp. attractive candidate for screening by PTT. Below the authors will describe a PTT capable of screening the entire coding region of **BRCA1** using 7 PCR per screen. The authors also show an example of a mutation in **BRCA1** detected using this assay.

L3 ANSWER 33 OF 34 MEDLINE DUPLICATE 19
AN 95330728 MEDLINE
DN 95330728 PubMed ID: 7606717
TI Mutation analysis of the **BRCA1** gene in ovarian cancers.
AU Takahashi H; Behbakht K; McGovern P E; Chiu H C; Couch F J; Weber B L; Friedman L S; King M C; Furusato M; LiVolsi V A; +
CS Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia.
SO CANCER RESEARCH, (1995 Jul 15) 55 (14) 2998-3002.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U14680
EM 199508
ED Entered STN: 19950828
Last Updated on STN: 19950828
Entered Medline: 19950817
AB Germline mutations of the **BRCA1** tumor suppressor gene on chromosome 17q are involved in a significant fraction of hereditary breast and ovarian cancers. Allelic deletions that include the **BRCA1** locus are common in breast and ovarian cancers, implying that somatic mutations of this gene may play an important role in the more common sporadic forms of these tumors as well. The recent cloning of **BRCA1** allows direct testing of this hypothesis. A combination of single strand conformation and sequencing analyses was used to examine the **22** coding **exons** and intronic splice donor and acceptor regions of **BRCA1** for mutations in 115 unselected cases of epithelial ovarian carcinoma. Seven mutations were identified, all of which were present in the germlines of patients with remarkable family or medical histories of breast and/or ovarian cancer. Eighty-nine of these tumors were examined for loss of heterozygosity in the **BRCA1** region of chromosome 17q, and 67% of the tumors studied exhibited allelic deletions that included this region. These data are consistent with the hypothesis that **BRCA1** mutations are involved in the etiology of hereditary ovarian carcinomas but occur rarely in sporadic tumors, and that the frequent allelic loss on chromosome 17q in this cancer type reflects the involvement of an additional tumor suppressor gene(s).

L3 ANSWER 34 OF 34 MEDLINE DUPLICATE 20
AN 96121595 MEDLINE
DN 96121595 PubMed ID: 8595420
TI Mutation analysis of the **BRCA1** gene in 76 Japanese ovarian cancer patients: four germline mutations, but no evidence of somatic

mutation.

AU Matsushima M; Kobayashi K; Emi M; Saito H; Saito J; Suzumori K; Nakamura Y
CS Laboratory of Molecular Medicine, University of Tokyo, Japan.

SO HUMAN MOLECULAR GENETICS, (1995 Oct) 4 (10) 1953-6.
Journal code: BRC; 9208958. ISSN: 0964-6906.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U14680
EM 199604
ED Entered STN: 19960424
Last Updated on STN: 19960424
Entered Medline: 19960418

AB To investigate the putative role of **BRCA1**, a gene involved in hereditary breast and ovarian cancer, in sporadic ovarian tumors among Japanese women, we examined 76 unselected primary ovarian cancers for mutations in the coding region of **BRCA1** using the single-strand conformation polymorphism technique. Although no somatic mutations were detected in any of the tumors, constitutional mutations were identified in four cases: two frameshifts, one nonsense mutation and one intronic base substitution 32 bp downstream of **exon 22**; RT-PCR experiments revealed that the single-base substitution in the intron seemed to increase the transcript lacking **exon 22**. All four cases were judged to involve truncation of the gene product. The evidence reported here supports a rather limited role of **BRCA1** in ovarian carcinogenesis in the Japanese population.

Japanese women, we examined 76 unselected primary ovarian cancers for mutations in the coding region of **BRCA1** using the single-strand conformation polymorphism technique. Although no somatic mutations were detected in any of the tumors, constitutional mutations were identified in four cases: two frameshifts, one nonsense mutation and one intronic base substitution 32 bp downstream of **exon 22**; RT-PCR experiments revealed that the single-base substitution in the intron seemed to increase the transcript lacking **exon 22**. All four cases were judged to involve truncation of the gene product. The evidence reported here supports a rather limited role of **BRCA1** in ovarian carcinogenesis in the Japanese population.

=> FIL STNGUIDE

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FULL ESTIMATED COST	13.97	14.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

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LAST RELOADED: May 24, 2002 (20020524/UP).

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